REMARKS

I. Support for claim amendments

Applicants have amended claim 1 to recite the limitation previously presented in dependent claim 3. Claims 2, 3, and 4 are hereby canceled. Support for the amendment to claim 1 may be found in the claims as originally filed and in the specification at, e.g., page 21, lines 15-18. Claim 34 is also amended to correct a typographical error. The word "of" in the third from last line in the claim has been replaced with the word "or." No new matter is added by these amendments. After entry of this amendment, claims 1 and 5-100 remain pending. Claims 10, 13, 14, 26-30, and 40-100 are presently withdrawn.

II. Obviousness-type double patenting rejection of claims 34-37

Applicants appreciate the Examiner's thoughtful consideration of the pending claims. On page 3 of the Office Action, the Examiner states that claims 34-37 are "provisionally rejected under the judicially created doctrine of obviousness-type double-patenting as being unpatentable over claim 42 of co-pending application Serial No. 10/525,301."[1] Specifically, the Examiner argues that:

> According to one interpretation, the claims of both applications permit the epitope to be that of a T helper; neither a CTL epitope, nor a B cell epitope is required. This interpretation is justified because in formula VI (claim 34), the "epitope" can be **either** a T helper **or** a CTL, notwithstanding the directive in part (i) of claim 34.

(emphasis in original). Applicants respectfully disagree with the Examiner's interpretation of the claims. Applicants respectfully submit that one skilled in the art would understand that the term "**and**" used in part (i)(a) of claim 34[2] requires that the polypeptide portion of the lipopeptide comprises **both** a T helper and a CTL. Formula (VI) shows two "epitope" moieties on the polypeptide portion of the lipopeptide, and the claim states that "epitope is a T-helper epitope or

[1] Applicants note that this application has since issued as U.S. Patent No. 7,569,225.

CTL epitope." In light of the unambiguous directive in part (i) of the claim, this statement can only be understood to mean that (1) the two epitopes in formula (VI) correspond to the two different epitopes referred to in part (i)(a) of the claim; and (2) it is not required that either epitope be linked to the central carbon via its amino or carboxyl group. Instead, Formula (VI) shows that the lipid moiety is attached via an internal lysine residue "that is positioned between the amino acid sequences of the T helper epitope **and** the CTL epitope." *See* specification at, e.g., page 15-18 (emphasis added); *see also* page 24, lines 15-28 (depicting Formula (VI) and stating that "the internal lysine … is positioned between the T-helper **and** CTL epitopes"(emphasis added)); page 24, lines 5-6 ("[n]aturally, it is **essential** to retain **both** T-helper function and CTL epitope function" (emphasis added)).

For the reasons set forth above, Applicants submit that one skilled in the art would understand the claimed lipopeptide to comprise **both** a T-helper epitope and CTL epitope. Claims 34-37 are therefore patentably distinct from claim 42 in the cited application (now claim 1 in the issued patent) because, by the same reasoning, claim 42 requires the presence of a B-cell epitope, not a CTL epitope. Withdrawal of the Examiner's provisional rejection is respectfully solicited.

III. Rejection of claims 1-3, 5 as obvious under 35 U.S.C. § 103 in view of Nardin (2008)

On pages 4-5 of the Office Action, the Examiner rejected claims 1-3 and 5 under 35 U.S.C. § 103 as being unpatentable over Nardin (1998). Specifically, the Examiner notes that the structures presented in Nardin's Figure 1B and Figure 1E render these claims obvious.

As noted above, Applicants have amended claim 1 to recite the limitation previously present in claim 3, *i.e.*, "wherein an internal lysine residue or internal lysine analog residue to which a lipid moiety is attached is positioned between the Th epitope and the CTL epitope." Claims 2, 3 and 4 are canceled. Claim 5 depends from claim 1 and is therefore also limited by the amendment to claim 1.

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[2] Part (i) of the claim states "said polypeptide comprises an amino acid sequence that comprises: (a) the amino acid sequence of a T helper cell (Th) epitope **and** the amino acid sequence of a CTL epitope, wherein said amino acid sequences are different."

Applicants respectfully submit that pending claims 1 and 5, as amended, are not obvious in view of Nardin. Nardin discloses branched constructs in which a lysine residue attached to the epitopes is positioned at the N-terminal end of the construct in a "template core". Figure 1E of Nardin (when read in conjunction with Figures 1B and 1C) shows that a lysine residue is located at the C-terminus of the "template core" comprising the two epitopes. However, Nardin does not disclose constructs wherein one of the two required epitopes (*i.e.*, the Th or CTL epitope) is located on the C-terminal side of an internal lysine residue *to which a lipid moiety is also attached*, and the other *different* epitope (i.e., the epitope type not present on the C-terminal side) is located *on the N-terminal* side of the lysine residue, as required by the amended claims. Further, the skilled person would not be motivated by the teaching provided in Nardin to construct the claimed molecule. Lipopeptide constructs known in the art (e.g., Nardin's construct) typically involve attachment of the lipid moiety to a residue at or near a terminus of the construct rather than to an internal residue located between the two different epitopes (for example, see Figure 1 of Nardin *et al.* (2001) *The Journal of Immunology* 166:481-489, previously presented to the Examiner in an IDS). Thus, Applicants respectfully submit that a *prima facie* case of obviousness has not been made with respect to Applicants' amended claims.

Applicants also submit that even if a *prima facie* case could be made, Applicants' have demonstrated sufficient unexpected results to rebut the argument and justify patentability. For example, one skilled in the art would not have expected that one could attach a lipid group to a lysine positioned *between* the two epitopes and achieve the markedly superior adjuvant effect demonstrated by applicants. In this regard, Applicants refer the Examiner to Figure 7 in the specification which, when read in conjunction with the disclosure at page 74, lines 12-21, demonstrates that constructs in which the lipid group attaches to an internal lysine residue positioned between the two epitopes (*i.e.* those constructs designated [Th]-Lys(Pam_1Cys-Ser-Ser)-[CTL], [Th]-Lys(Pam_2Cys-Ser-Ser)-[CTL], [Th]-Lys(Pam_3Cys-Ser-Ser)-[CTL], and [Th]-Lys($Chol_2$Lys-Ser-Ser)-[CTL]) were far better at eliciting a $CD8^+$ T cell response than a construct in which the lipid group is attached to the N-terminus (*i.e.* Pal_2LysLys[Th]-[CTL]). For all the forgoing reasons, withdrawal of the rejection of claims 1 and 5 in view of Nardin is earnestly solicited.

IV. Rejection of claim 1 as obvious under 35 U.S.C. § 103 in view of Tam (5,580,563), or in view of Tam and Sauzet

The Examiner also argues on pages 4-5 that claim 1 is obvious in view of Tam (U.S. Pat. No. 5,580,563) or, alternatively, in view of Tam and further in view of Sauzet (1995). Neither Tam nor Sauzet disclose lipopeptides wherein an internal lysine residue or internal lysine analog residue to which a lipid moiety is attached is positioned between the Th epitope and the CTL epitope, as required in Applicants' amended claim 1. A *prima facie* case of obviousness, therefore, has not been made with respect to Applicants' amended claim 1. Applicants respectfully solicit withdrawal of the rejection.

CONCLUSION

If the Examiner has any questions concerning this Response, the Examiner is invited to telephone Applicants' representative at (415) 875-2405.

Respectfully submitted,
DAVID JACKSON *ET AL.*

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By: /Chris Ullsperger/
Chris Ullsperger, Ph.D.
Reg. No.: 48,006
Fenwick & West LLP
Silicon Valley Center
801 California Street
Mountain View, CA 94041
Direct (415) 875-2405
Main (415) 875-2300
Fax (650) 938-5200